

PATENT COOPERATION TREATY

PCT

10/587313

INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY
(Chapter I of the Patent Cooperation Treaty)

(PCT Rule 44bis)

Applicant's or agent's file reference 38586-330001	FOR FURTHER ACTION	See item 4 below
International application No. PCT/US2005/002722	International filing date (<i>day/month/year</i>) 28 January 2005 (28.01.2005)	Priority date (<i>day/month/year</i>) 28 January 2004 (28.01.2004)
International Patent Classification (8th edition unless older edition indicated) See relevant information in Form PCT/ISA/237		
Applicant THE REGENTS OF THE UNIVERSITY OF CALIFORNIA		

1. This international preliminary report on patentability (Chapter I) is issued by the International Bureau on behalf of the International Searching Authority under Rule 44 *bis*.1(a).

2. This REPORT consists of a total of 5 sheets, including this cover sheet.

In the attached sheets, any reference to the written opinion of the International Searching Authority should be read as a reference to the international preliminary report on patentability (Chapter I) instead.

3. This report contains indications relating to the following items:

- | | | |
|-------------------------------------|--------------|---|
| <input checked="" type="checkbox"/> | Box No. I | Basis of the report |
| <input type="checkbox"/> | Box No. II | Priority |
| <input checked="" type="checkbox"/> | Box No. III | Non-establishment of opinion with regard to novelty, inventive step and industrial applicability |
| <input type="checkbox"/> | Box No. IV | Lack of unity of invention |
| <input checked="" type="checkbox"/> | Box No. V | Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement |
| <input type="checkbox"/> | Box No. VI | Certain documents cited |
| <input type="checkbox"/> | Box No. VII | Certain defects in the international application |
| <input type="checkbox"/> | Box No. VIII | Certain observations on the international application |

4. The International Bureau will communicate this report to designated Offices in accordance with Rules 44bis.3(c) and 93bis.1 but not, except where the applicant makes an express request under Article 23(2), before the expiration of 30 months from the priority date (Rule 44bis .2).

	Date of issuance of this report 31 July 2006 (31.07.2006)
The International Bureau of WIPO 34, chemin des Colombettes 1211 Geneva 20, Switzerland Facsimile No. +41 22 338 82 70	Authorized officer Simin Baharlou e-mail: pt09@wipo.int

PATENT COOPERATION TREATY

From the
INTERNATIONAL SEARCHING AUTHORITY

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REC'D 21 DEC 2005

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WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY

(PCT Rule 43bis.1)

Applicant's or agent's file reference 38586-330001		Date of mailing (day/month/year) 19 DEC 2005 FOR FURTHER ACTION See paragraph 2 below
International application No. PCT/US05/02722	International filing date (day/month/year) 28 January 2005 (28.01.2005)	Priority date (day/month/year) 28 January 2004 (28.01.2004)
International Patent Classification (IPC) or both national classification and IPC IPC(7): C07K 14/00; A61K 38/00, 39/395, C07H 21/04 and US Cl.: 530/350+, 300; 514/2; 536/23.1; 424/130.1		
Applicant THE REGENTS OF THE UNIVERSITY OF CALIFORNIA		

1. This opinion contains indications relating to the following items:

- ☒ Box No. I Basis of the opinion
- ☐ Box No. II Priority
- ☒ Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- ☐ Box No. IV Lack of unity of invention
- ☒ Box No. V Reasoned statement under Rule 43bis.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- ☐ Box No. VI Certain documents cited
- ☐ Box No. VII Certain defects in the international application
- ☐ Box No. VIII Certain observations on the international application

2. FURTHER ACTION

If a demand for international preliminary examination is made, this opinion will be considered to be a written opinion of the International Preliminary Examining Authority ("IPEA") except that this does not apply where the applicant chooses an Authority other than this one to be the IPEA and the chosen IPEA has notified the International Bureau under Rule 66.1bis(b) that written opinions of this International Searching Authority will not be so considered.

If this opinion is, as provided above, considered to be a written opinion of the IPEA, the applicant is invited to submit to the IPEA a written reply together, where appropriate, with amendments, before the expiration of 3 months from the date of mailing of Form PCT/ISA/220 or before the expiration of 22 months from the priority date, whichever expires later.

For further options, see Form PCT/ISA/220.

3. For further details, see notes to Form PCT/ISA/220.

Name and mailing address of the ISA/ US Mail Stop PCT, Attn: ISA/US Commissioner for Patents P.O. Box 1450 Alexandria, Virginia 22313-1450 Facsimile No. (571) 273-3201	Date of completion of this opinion 28 November 2005 (28.11.2005)	Authorized officer Suzanne M. Noakes, Ph.D. <i>Janie Ford</i> Telephone No. 571-272-1600 <i>for</i>
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Form PCT/ISA/237 (cover sheet) (April 2005)

WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY

International application No.

PCT/US05/02722

Box No. I Basis of this opinion

1. With regard to the language, this opinion has been established on the basis of:

- ☒ the international application in the language in which it was filed
- ☐ a translation of the international application into _____, which is the language of a translation furnished for the purposes of international search (Rules 12.3(a) and 23.1(b)).

2. With regard to any nucleotide and/or amino acid sequence disclosed in the international application and necessary to the claimed invention, this opinion has been established on the basis of:

a. type of material

- ☒ a sequence listing
- ☒ table(s) related to the sequence listing

b. format of material

- ☒ on paper
- ☒ in electronic form

c. time of filing/furnishing

- ☒ contained in the international application as filed.
- ☒ filed together with the international application in electronic form.
- ☐ furnished subsequently to this Authority for the purposes of search.

3. ☐ In addition, in the case that more than one version or copy of a sequence listing and/or table(s) relating thereto has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that in the application as filed or does not go beyond the application as filed, as appropriate, were furnished.

4. Additional comments:

WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY

International application No.

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Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non-obvious), or to be industrially applicable have not been examined in respect of:

- ☐ the entire international application
☒ claims Nos. 8-10 and 14-37

because:

- ☐ the said international application, or the said claim Nos. _____ relate to the following subject matter which does not require an international search (*specify*):

- ☐ the description, claims or drawings (*indicate particular elements below*) or said claims Nos. _____ are so unclear that no meaningful opinion could be formed (*specify*):

- ☐ the claims, or said claims Nos. _____ are so inadequately supported by the description that no meaningful opinion could be formed (*specify*):

- ☒ no international search report has been established for said claims Nos. 8-10 and 14-37

- ☐ a meaningful opinion could not be formed without the sequence listing; the applicant did not, within the prescribed time limit:

- ☐ furnish a sequence listing on paper complying with the standard provided for in Annex C of the Administrative Instructions, and such listing was not available to the International Searching Authority in a form and manner acceptable to it.

- ☐ furnish a sequence listing in electronic form complying with the standard provided for in Annex C of the Administrative Instructions, and such listing was not available to the International Searching Authority in a form and manner acceptable to it.

- ☐ pay the required late furnishing fee for the furnishing of a sequence listing in response to an invitation under Rules 13^{ter}.1(a) or (b).

- ☐ a meaningful opinion could not be formed without the tables related to the sequence listings; the applicant did not, within the prescribed time limit, furnish such tables in electronic form complying with the technical requirements provided for in Annex C-bis of the Administrative Instructions, and such tables were not available to the International Searching Authority in a form and manner acceptable to it.

- ☐ the tables related to the nucleotide and/or amino acid sequence listing, if in electronic form only, do not comply with the technical requirements provided for in Annex C-bis of the Administrative Instructions.

- ☐ See Supplemental Box for further details.

WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY

International application No.
PCT/US05/02722

Box No. V Reasoned statement under Rule 43 *bis*.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Claims <u>5-7</u>	YES
	Claims <u>1-4 and 12-13</u>	NO
Inventive step (IS)	Claims <u>NONE</u>	YES
	Claims <u>1-7 and 11-13</u>	NO
Industrial applicability (IA)	Claims <u>1-7 and 11-13</u>	YES
	Claims <u>NONE</u>	NO

2. Citations and explanations:

Claims 1-4 and 12-13 lack novelty under PCT Article 33(2) as being anticipated by Kiefer et al. (US 5,620,867 and EP 0 409 472). The instant invention is drawn to a 19 amino acid peptide derived from bone morphogenic protein (BMP), SEQ ID No: 1a. Kiefer et al. teach a 36 amino acid peptide of human bone morphogenic protein termed Exon 4. Amino acids 5-23 are 100% identical to SEQ ID No: 1a. Additionally, an isolated fragment of Exon 4 was obtained by tryptic digestion termed Peptide C and is a 12 amino acid fragment of Exon 4, which is 100% identical to SEQ ID No: 1a from amino acids 7-18. (See Figure's 2B of Kiefer et al., both US and EP). Thus Kiefer et al. teach peptides comprising SEQ ID No: 1a or fragments thereof. Pharmaceutical compositions of BMP are also taught which can contain other osteoinductive associated factors (see. Column 11, lines 4-17 of the US patent, and p. 8, lines 45-52 of the EP patent). The express statements in claims 1-7 and 11-13 which indicate properties, such as the peptide increases osteogenesis of BMP-2 is recognized as an inherent property of the Kiefer et al. peptides. Thus, claims 1-4 and 12-13 lack novelty.

Claims 1-7 and 11-13 lack an inventive step under PCT Article 33(3) as being obvious over Kiefer et al. (as cited above) in view of Carano et al. The teachings of Kiefer et al. are recited above.

However, what Keifer et al. fail to teach is the inclusion of the specific transforming growth factor-beta (TGF-beta) proteins in a composition comprising SEQ ID No: 1a or fragments thereof.

Carano et al. teach that members of the transforming growth factor superfamily include TGF-beta and BMP (to name just two). These often work in the same way because they often times share receptors and have high sequence homology (see. p. 984, 2nd column, 2nd paragraph). Furthermore, TGF-beta has been recognized as having a role in bone formation (p. 984, 2nd column, 3rd paragraph). BMP-2 and BMP-7 have been shown to promote bone repair (p. 985, 1st column, 1st paragraph) and/or ectopic bone formation (p. 985, 1st column, 3rd paragraph).

Thus, because Keifer et al. teach that their pharmaceutical compositions can also contain other osteoinductive associated factors, and Carano et al. establish that BMP-7, BMP-2 and TGF-beta are in fact osteoinductive proteins, then it would have been obvious to one of ordinary skill in the art to combine the peptide of Kiefer et al. with one of the osteoinductive proteins into a single composition. Consequently, the claims lack an inventive step.

Claims 1-7 and 11-13 meet the criteria set out in PCT Article 33(4), and thus possess industrial applicability because the subject matter claimed can be made or used in industry. The peptides, compositions and medicaments can be utilized in the biomedical field for bone regeneration/repair and thus would be useful in the medical field.